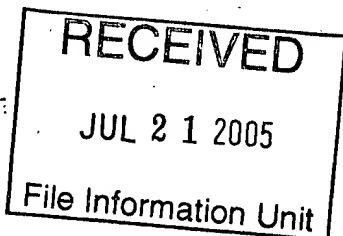


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US00655511B2

(12) **United States Patent**
Wallach et al.

(10) Patent No.: **US 6,555,111 B2**
(45) Date of Patent: **Apr. 29, 2003**

(54) **METHOD OF INHIBITING THE CYTOTOXIC EFFECT OF TNF WITH TNF RECEPTOR-SPECIFIC ANTIBODIES**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 23 days.

(21) Appl. No.: **09/800,909**

(22) Filed: **Mar. 8, 2001**

(65) **Prior Publication Data**

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Related U.S. Application Data

(60) Division of application No. 08/476,862, filed on Jun. 7, 1995, now Pat. No. 6,262,239, which is a continuation-in-part of application No. 08/321,685, filed on Oct. 12, 1994, now abandoned.

(30) **Foreign Application Priority Data**

Oct. 12, 1993 (IL) 107267

(51) Int. Cl.⁷ **A61K 39/395; C07K 16/28**

(52) U.S. Cl. **424/144.1; 424/130.1; 424/139.1; 424/141.1; 424/143.1; 424/152.1; 424/172.1; 530/387.1; 530/387.9; 530/388.1; 530/388.2; 530/388.22; 530/388.7**

(58) Field of Search **424/136.1, 133.1, 424/143.1, 145.1; 530/387.1, 388.1, 388.23**

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(57) **ABSTRACT**

Antibodies to Tumor Necrosis Factor receptors (TNF-Rs) which inhibit the cytotoxic effect of TNF but not its binding to the TNF-Rs, and ligands interacting with other receptors of the TNF/NGF family, are provided together with methods of producing them. The antibodies preferably bind to the fourth cysteine rich domain of the p75 TNF receptor or to the region between said fourth cysteine rich domain and the cell membrane.

3 Claims, 9 Drawing Sheets